

=> file medline, wpids, caplus, uspatfull

=> s "DMFO" or "difluoromethylornithine"

L1 4393 "DMFO" OR "DIFLUOROMETHYLORNITHINE"

=> s "decreas? spermine" or "decreas? spermidine"

L2 0 "DECREAS? SPERMINE" OR "DECREAS? SPERMIDINE"

=> s l1 and spermine

L3 1364 L1 AND SPERMINE

=> s l1 and spermidine

L4 1669 L1 AND SPERMIDINE

=> s l3 not py>2000

2 FILES SEARCHED...

L5 1137 L3 NOT PY>2000

=> s l5 and decreasing

L6 36 L5 AND DECREASING

=> s prostate and l5

L8 42 PROSTATE AND L5

=> d l8 1-42 ibib, abs

L8 ANSWER 1 OF 42 MEDLINE on STN

ACCESSION NUMBER: 2001067562 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 11082299

TITLE: Novel lysine-spermine conjugate inhibits polyamine transport and inhibits cell growth when given with DFMO.

AUTHOR: Weeks R S; Vanderwerf S M; Carlson C L; Burns M R; O'Day C L; Cai F; Devens B H; Webb H K

CORPORATE SOURCE: Oridigm Corporation, 4010 Stone Way North, No. 220, Seattle, Washington 98103, USA.. weeksrs@oridigm.com

SOURCE: Experimental cell research, (2000 Nov 25) Vol. 261, No. 1, pp. 293-302.

Journal code: 0373226. ISSN: 0014-4827.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200012

ENTRY DATE: Entered STN: 22 Mar 2001

Last Updated on STN: 22 Mar 2001

Entered Medline: 22 Dec 2000

AB Polyamines are ubiquitous molecules with multiple intracellular functions. Cells tightly regulate their levels through feedback mechanisms affecting synthesis, intracellular conversion, and transport. Because polyamines have an important role in regulating cell growth, they are a target for cancer therapeutic development. However, to effectively inhibit cell growth through polyamine depletion one needs to inhibit both polyamine synthesis and import. Although the mammalian polyamine transporter has not been cloned, we have identified ORI 1202, an N(1)-spermine -L-lysiny amide, as an effective polyamine transport inhibitor. ORI 1202 prevents the cellular accumulation of

[(3)H]spermidine over a 20-h test period. ORI 1202 (30-100 microM) effectively inhibits cell growth when used in conjunction with the polyamine synthesis inhibitor alpha- difluoromethylornithine (DFMO; > or =230 microM). Human breast, prostate, and bladder carcinoma cell lines and melanoma cell lines show ORI 1202 EC(50) values in the low micromolar range when tested in conjunction with DFMO. This cytostatic effect correlates with a reduction in the intracellular levels of putrescine and spermidine. When ORI 1202 (45 mg/kg, i.p., tidx5) and DFMO (1% in drinking water) were delivered over 14 days, MDA-MB-231 breast tumor xenografts in nude mice showed 50% growth inhibition. Polyamine depletion therapy provides a cytostatic therapy that could be useful against cancer and other diseases resulting from uncontrolled cell growth.
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L8 ANSWER 2 OF 42 MEDLINE on STN
ACCESSION NUMBER: 94300630 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 8028034
TITLE: Dose de-escalation chemoprevention trial of alpha-difluoromethylornithine in patients with colon polyps.
AUTHOR: Meyskens F L Jr; Emerson S S; Pelot D; Meshkinpour H; Shassetz L R; Einspahr J; Alberts D S; Gerner E W
CORPORATE SOURCE: Department of Medicine and Cancer Center, University of California at Irvine, Orange.
CONTRACT NUMBER: CA23074 (NCI)
CA30052 (NCI)
CA41108 (NCI)
SOURCE: Journal of the National Cancer Institute, (1994 Aug 3) Vol. 86, No. 15, pp. 1122-30.
Journal code: 7503089. ISSN: 0027-8874.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
(CONTROLLED CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199408
ENTRY DATE: Entered STN: 18 Aug 1994
Last Updated on STN: 29 Jan 1999
Entered Medline: 11 Aug 1994
AB BACKGROUND: alpha-Difluoromethylornithine (DFMO) is a potent inhibitor of carcinogenesis in experimental animal models. In these animal models, DFMO has been especially active in preventing carcinogen-induced epithelial cancers, including those of the skin, colon, breast, and urinary bladder. Although DFMO is known to exert its diverse biological effects by suppressing intracellular pools of the polyamines putrescine and spermidine, the precise mechanism by which polyamine depletion, induced by DFMO, suppresses carcinogenesis is unknown. PURPOSE: The specific aim of our study was to determine the lowest dose of DFMO that would deplete target tissue (colorectal mucosa) levels of these polyamines in humans who had undergone prior removal of colon polyps while producing minimal toxic effects. METHODS: A dose de-escalation chemoprevention trial of DFMO was conducted in 111 patients (36 female and 75 male) who were in generally good health, aged 39-79, and who had undergone colonoscopy for surgical removal of an adenomatous colon polyp greater than 3 mm within 5 years prior to entering the study. Groups of patients (12-20 patients per group) were orally treated with single, daily doses of DFMO ranging from 3.0 to 0.1 g/m2 for 4 weeks (28 days). Prior to initiation of DFMO treatment and at the end of treatment, six colorectal biopsy specimens were collected from each patient, along with serum samples.

All biopsies were performed between 9 AM and noon to avoid possible effects of diurnal variations in laboratory end points. Samples for analysis of plasma DFMO levels were also collected during this time period on the day after the last day of drug administration. RESULTS: DFMO caused a decrease in both putrescine content and the ratio of spermidine to spermine for all dose groups down to 0.25 g/m2. Both putrescine content and the ratio of spermidine to spermine and changes in these parameters as a function of DFMO treatment decreased as a function of donor age. None of the 30 patients receiving either 0.25 or 0.5 g/m2 experienced any clinical ototoxicity in this trial. CONCLUSIONS: DFMO is both safe and effective in reducing colorectal mucosal polyamine contents when it is administered orally to patients at doses as low as 0.25 g/m2 for 28 days. No ototoxicity was observed at doses up to twice this amount. IMPLICATIONS: If DFMO is also found to be effective in suppressing polyamine contents in other target tissues, it may be useful in preventing a wide range of human epithelial cancers, including those of the prostate and breast.

L8 ANSWER 3 OF 42 MEDLINE on STN
 ACCESSION NUMBER: 89269907 MEDLINE Full-text
 DOCUMENT NUMBER: PubMed ID: 3250232
 TITLE: Regulation of mammalian S-adenosylmethionine decarboxylase.
 AUTHOR: Pegg A E; Kameji T; Shirahata A; Stanley B; Madhubala R; Pajunen A
 CORPORATE SOURCE: Department of Physiology, Milton S. Hershey Medical Center, Pennsylvania State University College of Medicine, Hershey 17033.
 CONTRACT NUMBER: CA-18138 (NCI)
 SOURCE: Advances in enzyme regulation, (1988) Vol. 27, pp. 43-55.
 Journal code: 0044263. ISSN: 0065-2571.
 PUB. COUNTRY: ENGLAND: United Kingdom
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 198907
 ENTRY DATE: Entered STN: 9 Mar 1990
 Last Updated on STN: 6 Feb 1998
 Entered Medline: 3 Jul 1989

AB S-Adenosylmethionine decarboxylase is a key enzyme in the biosynthesis of polyamines that is the rate limiting step in the formation of spermidine and spermine. The activity of S-adenosylmethionine decarboxylase is known to be regulated negatively by these polyamines and positively by their precursor, putrescine. A specific antiserum to S-adenosylmethionine decarboxylase was raised by immunizing rabbits with the homogeneous enzyme purified from rat prostate and a specific radioimmunoassay for the protein was set up. Using this radioimmunoassay it was found that a number of inhibitors of other steps in the polyamine biosynthetic pathway lead to increases in the amount of S-adenosylmethionine decarboxylase protein. These changes were caused by both a decreased rate of degradation and an increased rate of synthesis of the protein. The increased synthesis was due to two factors; a rise in the amount of translatable mRNA and an enhanced translation efficiency. The mRNA content of the prostate was substantially increased by treatment for 3 days with alpha-difluoromethylornithine (2% in drinking water). The translation of mRNA for S-adenosylmethionine decarboxylase was studied using a polyamine-depleted reticulocyte lysate supplemented with mRNA from rat prostate and the antiserum to precipitate the proteins corresponding to S-adenosylmethionine decarboxylase. These studies indicated that the enzyme was synthesized as an inactive precursor of Mr 37,000 which was converted to the enzyme sub-unit of Mr 32,000. The conversion of the precursor to the active sub-unit in vitro was increased by putrescine. The precursor could also be detected by

immunoblotting of extracts from prostates of rats depleted of putrescine by treatment with the ornithine decarboxylase inhibitor, alpha-difluoromethylornithine. The translation of the S-adenosylmethionine decarboxylase mRNA in the reticulocyte lysates was strongly inhibited by the addition of spermidine or spermine demonstrating that polyamines directly inhibit the synthesis of S-adenosylmethionine decarboxylase. cDNA clones corresponding to S-adenosylmethionine decarboxylase were isolated using prostatic mRNA from polysomes enriched in S-adenosylmethionine decarboxylase by immunopurification. The use of these probes showed that rat ventral prostate contains two S-adenosylmethionine decarboxylase mRNA species of approximately 3.4 and 2.1 kb which differ in the 3' non-translated sequence. The sequence of these cDNAs will enable the amino acid sequence of the precursor to be obtained. This will provide evidence on the origin of the pyruvate prosthetic group of S-adenosylmethionine decarboxylase. (ABSTRACT TRUNCATED AT 400 WORDS)

L8 ANSWER 4 OF 42 MEDLINE on STN
 ACCESSION NUMBER: 88013021 MEDLINE Full-text
 DOCUMENT NUMBER: PubMed ID: 3116358
 TITLE: The effects of polyamine antimetabolites on polyamine-responsive casein kinase activity.
 AUTHOR: Levasseur S; Poleck T; Shaw M; Guinan P; Burke G
 CORPORATE SOURCE: Department of Medicine, Cook County Hospital, Chicago, IL 60612.
 CONTRACT NUMBER: AM 17561 (NIADDK)
 SOURCE: Life sciences, (1987 Oct 5) Vol. 41, No. 14, pp. 1679-83.
 Journal code: 0375521. ISSN: 0024-3205.
 PUB. COUNTRY: ENGLAND: United Kingdom
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 198710
 ENTRY DATE: Entered STN: 5 Mar 1990
 Last Updated on STN: 6 Feb 1998
 Entered Medline: 30 Oct 1987

AB The effects of two inhibitors of ornithine decarboxylase activity, alpha-difluoromethylornithine (DMFO) and (2R,5R) 6-heptyne-2,5 diamine (HDA), and an inhibitor of S-adenosylmethionine decarboxylase, methylglyoxal bis-guanylhyazone (MGBG), were tested on casein kinase activity and endogenous phosphorylation in the cytosol fractions of mouse thyroid and a rat prostate tumor model, Dunning R 3327 MAT LyLu subline. When tested at 5 mM, spermine, DMFO, HDA, and MGBG stimulated mouse thyroid casein kinase activity by 230%, 14%, 65% and 106%, respectively. Similar responses were observed in prostate tumor cytosol. In mouse thyroid cytosol, spermine stimulates 32P incorporation primarily into 3 proteins (MW: 107, 88, and 56 kDa). At 5 mM, MGBG partially reproduces the effects of spermine; HDA is less effective and DMFO is without effect. Similar effects were observed on 3 proteins in prostate tumor cytosol with molecular weights of 91, 41, and 32 kDa. These data provide additional support for the hypothesis that the observed synergistic inhibitory effect of DMFO and MGBG on cell growth may not be due solely to the inhibition of polyamine biosynthesis. Our findings suggest that MGBG-mediated reduction in the phosphorylation of casein kinase substrate should be considered as one locus of action.

L8 ANSWER 5 OF 42 MEDLINE on STN
 ACCESSION NUMBER: 88004668 MEDLINE Full-text
 DOCUMENT NUMBER: PubMed ID: 3115786
 TITLE: Phase I-II clinical trial with alpha-

difluoromethylornithine--an inhibitor of polyamine biosynthesis.

AUTHOR: Horn Y; Schechter P J; Marton L J
CORPORATE SOURCE: Department of Oncology, Assaf Harofeh Medical Center, Sackler School of Medicine, Zerifin, Israel.
CONTRACT NUMBER: CA-13525 (NCI)
CA-37606 (NCI)
SOURCE: European journal of cancer & clinical oncology, (1987 Aug) Vol. 23, No. 8, pp. 1103-7.
Journal code: 8112045. ISSN: 0277-5379.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: (CLINICAL TRIAL)
(CONTROLLED CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198711
ENTRY DATE: Entered STN: 5 Mar 1990
Last Updated on STN: 3 Feb 1997
Entered Medline: 20 Nov 1987

AB Alpha-difluoromethylornithine (DFMO) is an enzyme-activated, irreversible inhibitor of ornithine decarboxylase, the first enzyme in the synthesis of the polyamines putrescine, spermidine and spermine. DFMO has been shown to have a cytostatic and cytotoxic effect against various human tumor cell lines. The present study was designed to evaluate the toxicity and efficacy of this compound when administered orally at a dose of 1.7 g/m sq. t.i.d. added to conventional chemotherapy to 38 patients with carcinoma of the breast, stomach, prostate, female genital organs or metastatic carcinoma of unknown origin. A control group of 32 patients with similar malignancies received conventional chemotherapy only. Gastrointestinal, hematologic and biochemical abnormalities caused by DFMO were negligible. Reasonable ototoxicity was the major toxic effect caused by DFMO and resulted in discontinuation of therapy in 6 of 38 patients (15.8%). No differences in disease progression were seen between those patients receiving DFMO plus conventional chemotherapy and those receiving only conventional chemotherapy.

L8 ANSWER 6 OF 42 MEDLINE on STN
ACCESSION NUMBER: 87011854 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 3093695
TITLE: alpha-Difluoromethylornithine enhancement of 14C-putrescine uptake by an androgen-dependent prostatic tumor.
AUTHOR: Heston W D; Kadmon D
CONTRACT NUMBER: CA 00931 (NCI)
CA 33553 (NCI)
CA 34873 (NCI)
SOURCE: The Journal of urology, (1986 Oct) Vol. 136, No. 4, pp. 944-8.
Journal code: 0376374. ISSN: 0022-5347.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 198611
ENTRY DATE: Entered STN: 2 Mar 1990
Last Updated on STN: 3 Feb 1997
Entered Medline: 4 Nov 1986

AB Putrescine is a potential scanning agent for metastases of prostatic carcinoma. We examined the in vivo uptake of [14C]-putrescine by the Dunning

R3327H Copenhagen rat prostatic tumor and by other tissues, and conclude that: The uptake of [14C]-putrescine by the tumor was higher than that of the normal dorsolateral prostate, but similar to that of the ventral prostate. Tumor accumulation of [14C]-putrescine was enhanced 38% in intact and 45% in castrated animals by pretreatment with alpha-difluoromethylornithine (DFMO), a polyamine synthesis inhibitor. Further enhancement of tumor uptake (94% in intact and 201% in castrated animals) was achieved by combining DFMO pretreatment with androgen stimulation. Oral administration of methyl-glyoxal bis (guanyldihydrazone) (MGBG) increased intestinal uptake of [14C]-putrescine, while oral administration of unlabeled spermine and putrescine decreased it. Dexamethasone decreased the uptake of [14C]-putrescine by the spleen and intestine, but also reduced the prostatic uptake to a considerable extent. These observations are useful for the design of a putrescine-based scan for metastases of prostatic carcinoma.

L8 ANSWER 7 OF 42 MEDLINE on STN
 ACCESSION NUMBER: 86147796 MEDLINE Full-text
 DOCUMENT NUMBER: PubMed ID: 2419811
 TITLE: [Therapy with inhibitors of polyamine biosynthesis in refractory prostatic carcinoma. An experimental and clinical study].
 Therapie mit Inhibitoren der Polyaminbiosynthese beim refraktaren Prostatakarzinom. Eine experimentelle und klinische Studie.
 AUTHOR: Dunzendorfer U; Knoner M
 SOURCE: Onkologie, (1985 Aug) Vol. 8, No. 4, pp. 196-200.
 Journal code: 7808556. ISSN: 0378-584X.
 PUB. COUNTRY: Switzerland
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: German
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 198603
 ENTRY DATE: Entered STN: 21 Mar 1990
 Last Updated on STN: 6 Feb 1998
 Entered Medline: 31 Mar 1986

AB Transplantable prostate adenocarcinoma were treated with polyamine biosynthetic inhibitors. alpha-difluoromethylornithine (alpha-DFMO), an inhibitor of ornithine decarboxylase and by s-methylglyoxal-bisguanyldihydrazone (MGBG), an inhibitor of s-adenosylmethionine decarboxylase. The therapeutic regimen of 0.8-1.11 g/kg DFMO reduced the tumor growth by 40% whilst the combination with 10.5 mg/kg MGBG completely destroyed the prostate adenocarcinomas in the tumor-bearing animals. The polyamine content of spermidine and spermine in the cancerous tissues is significantly lower whereas the putrescine levels remain unchanged. The MGBG therapy distinctly stimulates the activity of ornithine decarboxylase and increases the putrescine concentration up to toxic levels. The application of alpha-DFMO prevented the toxic accumulation of putrescine and allowed higher doses of MGBG. Clinical trials with polyamine antimetabolites appeared useful due to pathological polyamine excretion of patients with metastatic prostate cancer. The therapy with 0.2-0.3 g/kg DFMO in patients with hormone-resistant prostate cancer and metastasis displayed a moderate anti-tumor activity following 2 months additional treatment. High levels of side effects, however, were registered and were similar to those of other cytotoxic compounds. A combined therapy with DFMO/MGBG in a patient with metastatic anaplastic prostate cancer did not improve the survival rate but showed regressive effects of the histological pattern.

L8 ANSWER 8 OF 42 MEDLINE on STN

ACCESSION NUMBER: 85261360 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 3926770
TITLE: Regulation of S-adenosylmethionine decarboxylase activity
in rat liver and prostate.
AUTHOR: Shirahata A; Pegg A E
CONTRACT NUMBER: CA18138 (NCI)
SOURCE: The Journal of biological chemistry, (1985 Aug 15) Vol.
260, No. 17, pp. 9583-8.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198509
ENTRY DATE: Entered STN: 20 Mar 1990
Last Updated on STN: 6 Feb 1998
Entered Medline: 16 Sep 1985

AB Two methods were used for the quantitation of S-adenosylmethionine decarboxylase protein. The first involved titrating the active site of the enzyme by reduction of the Schiff base between 3H-decarboxylated S-adenosylmethionine and the pyruvate prosthetic group with sodium cyanoborohydride. The second method was radioimmunoassay with rabbit antiserum which was used to determine the total immunoreactive enzyme protein. It was found that the increased S-adenosylmethionine decarboxylase activity produced in rat prostate by treatment with alpha-difluoromethylornithine and in both prostate and liver by methylglyoxal bis(guanylhydrazone) were due entirely to increases in the amount of enzyme protein. The ratio of enzyme activity to protein (measured by either method) remained constant in rats treated with the drugs. Treatment with 2% alpha-difluoromethylornithine in the drinking water for 3 days increased prostatic S-adenosylmethionine decarboxylase protein by 5-fold. A substantial part, but not all, of this increase could be accounted for by a slowing of the rate of degradation of the enzyme. The half-life for loss of activity and titratable protein after inhibition of protein synthesis by cycloheximide was increased from 35 to 108 min by treatment with alpha-difluoromethylornithine. However, the half-life for loss of immunoreactive protein which was considerably longer was only increased from 139 to 213 min. The molecular weight of the S-adenosylmethionine decarboxylase subunit determined by immunoblotting was 32,000, and no smaller immunoreactive fragments were detected. These results indicate that spermidine depletion produced by alpha-difluoromethylornithine affects the degradation of S-adenosylmethionine decarboxylase at an early step involving the loss of the active site without substantial breakdown of the protein.

L8 ANSWER 9 OF 42 MEDLINE on STN
ACCESSION NUMBER: 84256587 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 6430275
TITLE: Differential effects of 2-difluoromethylornithine
and methylglyoxal bis(guanylhydrazone) on the
testosterone-induced growth of ventral prostate
and seminal vesicles of castrated rats.
AUTHOR: Kapyaho K; Kallio A; Janne J
SOURCE: The Biochemical journal, (1984 May 1) Vol. 219, No. 3, pp.
811-7.
Journal code: 2984726R. ISSN: 0264-6021.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals

ENTRY MONTH: 198408
ENTRY DATE: Entered STN: 20 Mar 1990
Last Updated on STN: 20 Mar 1990
Entered Medline: 8 Aug 1984

AB 2-Difluoromethylornithine totally prevented any increases in putrescine and spermidine concentrations in the ventral prostate of castrated rats during a 6-day testosterone treatment. Prostatic ornithine decarboxylase activity was inhibited by 80%, whereas S-adenosylmethionine decarboxylase was stimulated by more than 9-fold. In seminal vesicle, the inhibition of putrescine and spermidine accumulation, as well as of ornithine decarboxylase activity, was only minimal, and no stimulation of S-adenosylmethionine decarboxylase was observed. Administration of methylglyoxal bis(guanylhydrazone) to castrated androgen-treated rats resulted in a marked increase in concentrations of all prostatic polyamines. Prostatic ornithine decarboxylase activity was nearly 2 times and adenosylmethionine decarboxylase activity 9 times higher than that of the testosterone-treated animals. In contrast with ventral prostate, methylglyoxal bis(guanylhydrazone) treatment inhibited moderately the accumulation of spermidine and spermine in seminal vesicle, although both ornithine decarboxylase and S-adenosylmethionine decarboxylase activities were stimulated. Difluoromethylornithine inhibited significantly the weight gain of ventral prostate, but methylglyoxal bis(guanylhydrazone) produced a substantial increase in prostatic weight. These changes were largely due to the fact that the volume of prostatic secretion was greatly decreased by difluoromethylornithine, whereas methylglyoxal bis(guanylhydrazone) increased the amount of secretion. Treatment with difluoromethylornithine strikingly increased the methylglyoxal bis(guanylhydrazone) content of both ventral prostate and seminal vesicle, but even under these conditions the drug concentration remained low in comparison with other tissues. The results indicate that a combined use of these two polyamine anti-metabolites does not necessarily result in a synergistic growth inhibition of the androgen-induced growth of male accessory sexual glands.

L8 ANSWER 10 OF 42 MEDLINE on STN

ACCESSION NUMBER: 84106552 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 6420052

TITLE: Differential effect of alpha-difluoromethylornithine on the in vivo uptake of ¹⁴C-labeled polyamines and methylglyoxal bis(guanylhydrazone) by a rat prostate-derived tumor.

AUTHOR: Heston W D; Kadmon D; Covey D F; Fair W R

CONTRACT NUMBER: 2507-RR05389 (NCRR)

CA 33553 (NCI)

CA 34873 (NCI)

+

SOURCE: Cancer research, (1984 Mar) Vol. 44, No. 3, pp. 1034-40.

Journal code: 2984705R. ISSN: 0008-5472.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 198403

ENTRY DATE: Entered STN: 19 Mar 1990

Last Updated on STN: 3 Feb 1997

Entered Medline: 23 Mar 1984

AB The uptake of exogenously administered radiolabeled polyamines by a rat prostate-derived tumor line, the Dunning R3327 MAT-Lu, and various normal tissues was studied. Pretreatment of tumor cells in vitro with alpha-difluoromethylornithine (DFMO), a polyamine synthesis inhibitor, resulted in a

markedly enhanced uptake of both [14C]putrescine and [14 C]spermidine. The in vitro uptake of [14C]putrescine by these cells was effectively inhibited by unlabeled spermine, spermidine, 1,8-diaminooctane, 1,7-diaminoheptane, 1,6-diaminohexane, 1,5-diaminopentane, 1,4-diaminopentane, and 1,4-diaminobutane, but less effectively by 1,4-diamino-2,3-butene and 1,4-diamino-2,3-butyne. The diamines, 1,3-diaminopropane and 1,2-diaminoethane, were ineffective in inhibiting [14C]putrescine uptake in vitro into the R3327 MAT-Lu cell line. When tumor-bearing animals were pretreated with DFMO or with DFMO and 5-alpha-dihydrotestosterone propionate, the tumor and prostate uptake of [14C]putrescine and [14C]-cadaverine was enhanced but not substantially increased in other tissues. In contrast to the in vitro results, spermidine and spermine were not enhanced substantially by DFMO pretreatment into any tissue, and their uptake into the tumor actually decreased. Ethylenediamine, which does not utilize the polyamine transport system, did not have its uptake increased into any tissue following DFMO pretreatment. The chemotherapeutic agent, methylglyoxal bis(guanylhydrazine), which utilizes the polyamine transport system for uptake into cells, exhibited uptake behavior different from that of the polyamines. Thus, methylglyoxal bis(guanylhydrazine) uptake into the tumor was not significantly increased or decreased by DFMO or by DFMO + 5-alpha-dihydrotestosterone propionate pretreatment, and only the ventral, but not the dorsal-lateral, lobe of the prostate showed increased uptake of methylglyoxal bis(guanylhydrazine) following DFMO + 5-alpha-dihydrotestosterone propionate pretreatment.

L8 ANSWER 11 OF 42 MEDLINE on STN

ACCESSION NUMBER: 84106371 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 6420041

TITLE: Potentiation of methylglyoxal-bis-guanylhydrazine by alpha-difluoromethylornithine in rat prostate cancer.

AUTHOR: Herr H W; Kleinert E L; Relyea N M; Whitmore W F Jr

CONTRACT NUMBER: CA 08748 (NCI)

SOURCE: Cancer, (1984 Mar 15) Vol. 53, No. 6, pp. 1294-8.
Journal code: 0374236. ISSN: 0008-543X.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals

ENTRY MONTH: 198403

ENTRY DATE: Entered STN: 19 Mar 1990
Last Updated on STN: 3 Feb 1997
Entered Medline: 23 Mar 1984

AB The polyamines, putrescine, spermidine, and spermine, are fundamentally related to both normal and neoplastic cell proliferation. The prostate gland and prostatic tumors in man and rodents contain large amounts of polyamines. This suggests that inhibition of polyamine biosynthetic enzymes, ornithine decarboxylase (ODC) and S-adenosyl-methionine decarboxylase (SAMDC) may retard the growth of prostatic cancer. Since alpha-difluoromethylornithine (DFMO) and methylglyoxal-bis-guanylhydrazine (MGBG) are irreversible and competitive inhibitors of ODC and SAMDC, respectively, they were tested as single agents and in combination on a transplantable rapidly growing and hormone-resistant G subline of the Dunning R-3327 rat prostatic adenocarcinoma. Groups of rats bearing tumors were treated with various regimens of DFMO, MGBG, and DFMO plus MGBG, daily for 21 days. Analysis of differences in tumor growth between treatment groups and controls showed DFMO had no antitumor effect but was well tolerated, MGBG retarded growth rate significantly but resulted in drug deaths in over 50% of the animals, and the combination of DFMO and MGBG resulted in rapid decline in tumor growth rates after 5 to 9 days of treatment with reduced toxicity. At 21 days, or death, 38 of 60 (63%) rats had no viable

tumor on histologic study, whereas tumor was present in each of the animals in the other groups. Alpha-difluoromethylornithine increased the intracellular uptake of MGBG and potentiated the antigrowth activity of MGBG on a hormone refractory rat prostatic tumor with less toxicity than MGBG alone.

L8 ANSWER 12 OF 42 MEDLINE on STN

ACCESSION NUMBER: 83121486 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 6186061

TITLE: [Therapy of prostate carcinoma with polyamine synthesis inhibitors. I. Physiological and pathophysiological principles].
Therapie des Prostatakarzinoms mit Polyaminsyntheseinhibitoren. I. Physiologische und pathophysiologische Grundlagen.

AUTHOR: Dunzendorfer U

SOURCE: Urologia internationalis, (1982) Vol. 37, No. 5, pp. 349-57.

Journal code: 0417373. ISSN: 0042-1138.

PUB. COUNTRY: Switzerland

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: German

FILE SEGMENT: Priority Journals

ENTRY MONTH: 198303

ENTRY DATE: Entered STN: 18 Mar 1990

Last Updated on STN: 18 Mar 1990

Entered Medline: 17 Mar 1983

AB The therapeutic concept of irreversible inhibition of both ornithine decarboxylase (ODC) and S-adenosylmethionine decarboxylase (SAMDC) by alpha-difluoromethylornithine (DFMO) and methylglyoxal bis-guanylhydrazine (MGBG) is based on pathologic activities of these enzymes in tumor tissue. The polyamines putrescine, spermidine and spermine are measured in highest concentration in the prostate of both men and animals, with a significant increase of spermine in benign hyperplasia of the prostate. Patients with metastatic cancer of the prostate have elevated putrescine levels in the 24-hour urine. Treatment with 3 or 1% DFMO or 11 mg/kg MGBG in transplantable human and experimental cancer of the prostate demonstrated a significant anti-growth effect. A combination of DFMO and MGBG is tumor-destructive. The combination of 1% DFMO and 11 mg/kg MGBG distinctly reduces the activity of ODC and SAMDC and significantly lowers the levels of putrescine, spermidine and spermine in the tumor.

L8 ANSWER 13 OF 42 MEDLINE on STN

ACCESSION NUMBER: 82206053 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 6177318

TITLE: Effect on prostatic growth of 2-difluoromethylornithine, an effective inhibitor of ornithine decarboxylase.

AUTHOR: Danzin C; Claverie N; Wagner J; Grove J; Koch-Weser J

SOURCE: The Biochemical journal, (1982 Jan 15) Vol. 202, No. 1, pp. 175-81.

Journal code: 2984726R. ISSN: 0264-6021.

PUB. COUNTRY: ENGLAND: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 198207

ENTRY DATE: Entered STN: 17 Mar 1990

Last Updated on STN: 17 Mar 1990

Entered Medline: 8 Jul 1982

AB 2-Difluoromethylornithine (DFMO), an enzyme-activated irreversible inhibitor of ornithine decarboxylase, causes marked changes in the polyamine metabolism of ventral prostate when given to adult rats in drinking water (20 g/l) for 3 consecutive days. A 90% inhibition of ornithine decarboxylase activity is accompanied by approx. 80% decreases of the concentrations of putrescine and spermidine and by a 36% decrease in spermine. Concomitantly, S-adenosylmethionine decarboxylase activity increases 7-fold and the concentration of decarboxylated S-adenosylmethionine 450-fold. When DFMO is given to immature rats for 12 consecutive days the above described changes are accompanied by a marked reduction in the age-dependent increases of the wet weight and RNA and DNA contents of the ventral prostate. In adult rats DFMO decreases the weight and RNA content of the ventral prostate within 4 days by 32% and 24% respectively and maintains them constant for the next 19 days. After 23 days of treatment, the prostatic weight is 46% of that of control animals of the same age, whereas the weights of other organs are only slightly decreased. Cytological studies carried out at this time show that DFMO reduces the size of both prostatic acini and the epithelial cells lining the acini.

L8 ANSWER 14 OF 42 MEDLINE on STN

ACCESSION NUMBER: 82186722 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 6804235

TITLE: Accumulation of decarboxylated S-adenosyl-L-methionine in mammalian cells as a consequence of the inhibition of putrescine biosynthesis.

AUTHOR: Mamont P S; Danzin C; Wagner J; Siat M; Joder-Ohlenbusch A M; Claverie N

SOURCE: European journal of biochemistry / FEBS, (1982 Apr) Vol. 123, No. 3, pp. 499-504.

Journal code: 0107600. ISSN: 0014-2956.

PUB. COUNTRY: GERMANY, WEST: Germany, Federal Republic of

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 198207

ENTRY DATE: Entered STN: 17 Mar 1990

Last Updated on STN: 6 Feb 1998

Entered Medline: 19 Jul 1982

AB Biological transmethylation reactions and polyamine biosynthesis share the substrate S-adenosyl-L-methionine. Under normal conditions, decarboxylated S-adenosyl-L-methionine, the aminopropyl donor for polyamine biosynthesis, does not accumulate because of its rapid utilization in spermidine and spermine synthesis. Alteration of polyamine synthesis by DL-alpha-difluoromethylornithine, an enzyme-activated irreversible inhibitor of L-ornithine decarboxylase, leads to a striking accumulation of decarboxylated S-adenosyl-L-methionine in rat hepatoma cells cultured in vitro and in rat ventral prostate. This increase is due both to lack of putrescine and spermidine for the aminopropyltransferase reactions and to the elevation of S-adenosyl-L-methionine decarboxylase activity. The biological implications of accumulation of decarboxylated S-adenosyl-L-methionine are discussed with regard to the regulation of S-adenosyl-L-methionine decarboxylase activity and to the antiproliferative effects of DL-alpha-difluoromethylornithine.

L8 ANSWER 15 OF 42 MEDLINE on STN

ACCESSION NUMBER: 79156030 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 431333

TITLE: Effect of alpha-difluoromethylornithine, an enzyme-activated irreversible inhibitor of ornithine

decarboxylase, on polyamine levels in rat tissues.
AUTHOR: Danzin C; Jung M J; Grove J; Bey P
SOURCE: Life sciences, (1979 Feb 5) Vol. 24, No. 6, pp. 519-24.
Journal code: 0375521. ISSN: 0024-3205.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197906
ENTRY DATE: Entered STN: 15 Mar 1990
Last Updated on STN: 15 Mar 1990
Entered Medline: 11 Jun 1979

L8 ANSWER 16 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:120148 CAPLUS Full-text
DOCUMENT NUMBER: 135:116720
TITLE: Polyamine depletion therapy in prostate cancer
AUTHOR(S): Devens, B. H.; Weeks, R. S.; Burns, M. R.; Carlson, C. L.; Brawer, M. K.
CORPORATE SOURCE: Oridigm Corporation, Seattle, WA, 98133, USA
SOURCE: Prostate Cancer and Prostatic Diseases (2000), 3(4), 275-279
CODEN: PCPDFW; ISSN: 1365-7852
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The prostate gland has among the highest level of polyamines in the body and prostate carcinomas have even higher polyamine concns. Attempts to limit tumor growth by inhibition of polyamine synthesis have not been very successful since cells have the capacity to take up polyamines from the blood. This work reports studies utilizing polyamine depletion by means of a combination of blockade of polyamine synthesis with DFMO (α -difluoromethylornithine), an inhibitor of ornithine decarboxylase, the rate-limiting enzyme in the polyamine-synthetic pathway, and ORI 1202, a novel inhibitor of polyamine transport into the cell. This cytostatic combination, even in the presence of excess extracellular polyamines, slowed the growth of the human prostate tumor cell line PC-3 grown in tissue culture, with an EC50 in the micromolar range. Other prostate cell lines were similarly growth inhibited, including LNCaP.FGC and DU145. Growth of the PC-3 tumor cell line as a xenograft in nude mice was also slowed by this combination of compds. Polyamine concns. in the tumor were lowered from control values. This combination therapy could provide an effective and potentially nontoxic therapy for prostate tumors.

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 17 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:808449 CAPLUS Full-text
DOCUMENT NUMBER: 134:141470
TITLE: Novel lysine-spermine conjugate inhibits polyamine transport and inhibits cell growth when given with DFMO
AUTHOR(S): Weeks, Reitha S.; Vanderwerf, Scott M.; Carlson, C. Lance; Burns, Mark R.; O'Day, Christine L.; Cai, Feng; Devens, Bruce H.; Webb, Heather K.
CORPORATE SOURCE: Oridigm Corporation, Seattle, WA, 98103, USA
SOURCE: Experimental Cell Research (2000), 261(1), 293-302
CODEN: ECREAL; ISSN: 0014-4827
PUBLISHER: Academic Press

DOCUMENT TYPE: Journal
LANGUAGE: English

AB Polyamines are ubiquitous mols. with multiple intracellular functions. Cells tightly regulate their levels through feedback mechanisms affecting synthesis, intracellular conversion, and transport. Because polyamines have an important role in regulating cell growth, they are a target for cancer therapeutic development. However, to effectively inhibit cell growth through polyamine depletion one needs to inhibit both polyamine synthesis and import. Although the mammalian polyamine transporter has not been cloned, we have identified ORI 1202, an N1-spermine -L-lysiny amide, as an effective polyamine transport inhibitor. ORI 1202 prevents the cellular accumulation of [3H]spermidine over a 20-h test period. ORI 1202 (30-100 μ M) effectively inhibits cell growth when used in conjunction with the polyamine synthesis inhibitor α -difluoromethylornithine (DFMO; ≥ 230 μ M). Human breast, prostate, and bladder carcinoma cell lines and melanoma cell lines show ORI 1202 EC50 values in the low micromolar range when tested in conjunction with DFMO. This cytostatic effect correlates with a reduction in the intracellular levels of putrescine and spermidine. When ORI 1202 (45 mg/kg, i.p., tidx5) and DFMO (1% in drinking water) were delivered over 14 days, MDA-MB-231 breast tumor xenografts in nude mice showed 50% growth inhibition. Polyamine depletion therapy provides a cytostatic therapy that could be useful against cancer and other diseases resulting from uncontrolled cell growth. (c) 2000 Academic Press.

REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 18 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:704169 CAPLUS Full-text

DOCUMENT NUMBER: 130:119152

TITLE: Phase I chemoprevention study of piroxicam and α -difluoromethylornithine

AUTHOR(S): Carbone, Paul P.; Douglas, Jeffrey A.; Larson, Paul O.; Verma, Ajit K.; Blair, Ian A.; Pomplun, Marcia; Tutsch, Kendra D.

CORPORATE SOURCE: Department of Medicine, University of Wisconsin Comprehensive Cancer Center, Madison, WI, 53792, USA

SOURCE: Cancer Epidemiology, Biomarkers & Prevention (1998), 7(10), 907-912

CODEN: CEBPE4; ISSN: 1055-9965

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A two-step Phase I study of piroxicam (PXM) and α -fluoromethylornithine (DFMO) alone and in combination was initiated to assess toxicity and the impact of these drugs on several biol. markers. In step 1, 12 subjects with a history of skin cancers were assigned to receive PXM 10 mg every day (q.d.) or 10 mg every other day (q.o.d.) The dosage of PXM 10 mg q.o.d. was tolerated. No changes were seen in 12-O-tetradecanoylphorbol-13-acetate (TPA)-induced ornithine decarboxylase (ODC) or urinary polyamine levels. Steady-state serum levels of PXM were consistent with the oral dose level. In step 2, 31 subjects with stage 0 or I nonmelanoma skin cancers, stage A or B prostate or colon cancer, or stage I breast cancer or who had a family history of cancer were randomized to receive DFMO 0.5 g/m², PXM 10 mg q.o.d., or the combination of DFMO and PXM. In addition to the biol. markers of TPA-induced ODC activity in skin biopsies and urinary polyamine levels, we measured urinary 11-dehydrothromboxane B2, a specific metabolite of thromboxane A2. Of the 12 subjects on DFMO/PXM, 2 dropped out for non-drug-related reasons. Three developed grade-2 drug-related toxicities. One subject developed dyspnea that resolved and was able to continue on the study for 6 mo. One subject who

developed diarrhea that resolved after 5 days was also able to restart the drug without a recurrence. A third subject described intermittent episodes of tinnitus starting 4 h after taking PXM that lasted only 5 s and did not progress on treatment. Comparing the 6-mo measurements with pretreatment, DFMO/PXM or DFMO significantly reduced TPA-induced ODC levels (Ps, 0.03 and 0.05). Urinary polyamine levels of spermidine decreased slightly with the DFMO/PXM or DFMO alone, whereas putrescine decreased with PXM alone. Levels of 11-dehydrothromboxane B2 were depressed by PXM and PXM/DFMO. The doses of DFMO/PXM determined in step 2 are potential starting dosages for Phase IIa and IIb chemoprevention trials.

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 19 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1987:568394 CAPLUS Full-text

DOCUMENT NUMBER: 107:168394

TITLE: The effects of polyamine antimetabolites on polyamine-responsive casein kinase activity

AUTHOR(S): Levasseur, S.; Poleck, T.; Shaw, M.; Guinan, P.; Burke, G.

CORPORATE SOURCE: Dep. Med., Cook Cty. Hosp., Chicago, IL, 60612, USA

SOURCE: Life Sciences (1987), 41(14), 1679-83

CODEN: LIFSAK; ISSN: 0024-3205

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The effects of two inhibitors of ornithine decarboxylase activity, α -difluoromethylornithine (DMFO) and (2R,5R)-6-heptyne-2,5 diamine (HDA), and an inhibitor of S-adenosylmethionine decarboxylase, methylglyoxal bis-guanylhydrazone (MGBG), were tested on casein kinase activity and endogenous phosphorylation in the cytosol fractions of mouse thyroid and a rat prostate tumor model, Dunning R 3327 MAT LyLu subline. When tested at 5 mM, spermine, DMFO, HDA, and MGBG stimulated mouse thyroid casein kinase activity by 230%, 14%, 65% and 106%, resp. Similar responses were observed in prostate tumor cytosol. In mouse thyroid cytosol, spermine stimulated ³²P incorporation primarily into 3 proteins (mol. weight: 107, 88, and 56 kDa). At 5 mM, MGBG partially reproduced the effects of spermine; HDA was less effective and DMFO was without effect. Similar effects were observed on 3 proteins in prostate tumor cytosol with mol. wts. of 91, 41, and 32 kDa. These data provide addnl. support for the hypothesis that the observed synergistic inhibitory effect of DMFO and MGBG on cell growth may not be due solely to the inhibition of polyamine biosynthesis. MGBG-mediated reduction in the phosphorylation of casein kinase substrate should be considered as one locus of action.

L8 ANSWER 20 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1985:605815 CAPLUS Full-text

DOCUMENT NUMBER: 103:205815

TITLE: Prostatic tumor suppression with a combination of α -difluoromethylornithine and methylglyoxal-bis-(guanylhydrazone)

AUTHOR(S): Herr, Harry W.

CORPORATE SOURCE: Urol. Oncol. Res. Lab., Mem. Sloan-Kettering Cancer Cent., New York, NY, USA

SOURCE: Surgical Forum (1985), 36, 648-51

CODEN: SUFOAX; ISSN: 0071-8041

DOCUMENT TYPE: Journal

LANGUAGE: English

AB In rats bearing prostatic tumors, tumor growth inhibition and enhanced survival was observed with combined treatment with α -difluoromethylornithine (DFMO)

[70052-12-9] and methylglyoxal-bis-(guanylhyazone (MGBG) [459-86-9]. DFMO priming for 7 days prior to pulse MGBG treatment resulted in a median tumor volume of 0.06 mL and no palpable tumor in 80% of the rats after 21 days of MGBG treatment. Retreatment of rats bearing growing tumors retarded tumor growth sequentially and lengthened survival time. The combination chemotherapy lowered the tumor levels of putrescine [110-60-1], spermidine [124-20-9], and spermine [71-44-3]. Also [14C] MGBG was preferentially taken up by tumor cells exposed to DFMO. Electron microscopy suggested selective MGBG uptake and a cytotoxic effect on mitochondria.

L8 ANSWER 21 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1985:590106 CAPLUS Full-text

DOCUMENT NUMBER: 103:190106

TITLE: Effect of estrogen and androgen administration on α -difluoromethylornithine-enhanced putrescine uptake by the rat prostate

AUTHOR(S): Kadmon, D.; Mahle, C.; Heston, W. D. W.; Hahn, D. A.

CORPORATE SOURCE: Sch. Med., Washington Univ., St. Louis, MO, 63110, USA

SOURCE: Prostate (New York, NY, United States) (1985), 6(4), 343-9

CODEN: PRSTDS; ISSN: 0270-4137

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Pharmacol. castration of adult rats with DES [56-53-1] decreased ¹⁴C-labeled putrescine [110-60-1] uptake by ventral prostate and this effect was antagonized by 5 α -dihydrotestosterone [521-18-6] or α -difluoromethylornithine (DFMO) [70052-12-9]. However, dramatic increases in prostate uptake of exogenously administered putrescine were observed on treatment with DES, androgen, and DFMO. Small bowel uptake of putrescine was markedly increased by DFMO as was uptake in other organs (kidney, liver, spleen) but estrogen and androgen had no marked effect on the polyamine uptake in these organs. Treatment with DES alone decreased the wet weight as well as the ornithine decarboxylase [9024-60-6], spermidine [124-20-9], and spermine [71-44-3] levels in prostate. The most dramatic decrease in spermine and spermidine prostate levels was produced by treatment with DES, androgen, and DFMO. Estrogen, androgen, and DFMO treatment may be useful in enhancing uptake of labeled putrescine in human prostate and prostate-derived tumors and consequently in the imaging of soft tumor metastases of prostate origin.

L8 ANSWER 22 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1985:589316 CAPLUS Full-text

DOCUMENT NUMBER: 103:189316

TITLE: Therapy with inhibitors of polyamine biosynthesis in refractory prostate carcinoma. An experimental and clinical study

AUTHOR(S): Dunzendorfer, U.; Knoener, M.

CORPORATE SOURCE: Abt. Urol., Johann-Wolfgang-Von-Goethe-Univ., Frankfurt/Main, Fed. Rep. Ger.

SOURCE: Onkologie (1985), 8(4), 196-200

CODEN: ONKOD2; ISSN: 0378-584X

DOCUMENT TYPE: Journal

LANGUAGE: German

AB Exptl. animals with human transplantable prostate adenocarcinoma were treated with polyamine biosynthetic inhibitors α -difluoromethylornithine (α -DFMO) [70052-12-9], and inhibitor of ornithine decarboxylase, and s-methylglyoxalbiscguanylhyazone (MGBG) [459-86-9], an inhibitor of s-adenosylmethionine decarboxylase. The therapeutic regimen of 0.8-1.11 g/kg DFMO

reduced the tumor growth by 40%, whereas the combination of DFMO and 10.5 mg/kg MGBG completely destroyed the prostate adenocarcinomas in the tumor-bearing animals. In the cancerous tissue the content of spermidine and spermine is significantly lower whereas the putrescine levels remained unchanged as a result of treatment. The MGBG therapy alone stimulates the activity of ornithine decarboxylase and increases the putrescine concentration up to toxic levels in tissues. The application of α -DFMO prevented the toxic accumulation of putrescine and allowed higher doses of MGBG to be used. The therapy with 0.2-0.3 g/kg DFMO in patients with hormone-resistant prostate cancer and metastasis produced moderate antitumor effects after 2 mo; side effects, however, were observed and were similar to those of other cytotoxic compds. A combined therapy with DFMO/MGBG in a patient with metastatic anaplastic prostate cancer did not improve the survival rate but regressive effects were noted in the histol. pattern of the prostate carcinoma.

L8 ANSWER 23 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1984:400353 CAPLUS Full-text

DOCUMENT NUMBER: 101:353

TITLE: Differential effects of 2-difluoromethylornithine and methylglyoxal bis(guanylhydrazone) on the testosterone-induced growth of ventral prostate and seminal vesicles of castrated rats

AUTHOR(S): Kapyaho, Kirsti; Kallio, Arja; Janne, Juhani

CORPORATE SOURCE: Dep. Biochem., Univ. Helsinki, Helsinki, SF-00170/17, Finland

SOURCE: Biochemical Journal (1984), 219(3), 811-17

CODEN: BIJOAK; ISSN: 0306-3275

DOCUMENT TYPE: Journal

LANGUAGE: English

AB 2-Difluoromethylornithine [70052-12-9] totally prevented any increases in putrescine [110-60-1] and spermidine [124-20-9] concns. in the ventral prostate of castrated rats during a 6-day testosterone [58-22-0] treatment. Prostatic ornithine decarboxylase [9024-60-6] activity was inhibited by 80%, whereas S-adenosylmethionine decarboxylase [9036-20-8] was stimulated >9-fold. In seminal vesicle, the inhibition of putrescine and spermidine accumulation, as well as of ornithine decarboxylase activity, was only minimal, and no stimulation of S-adenosylmethionine decarboxylase was observed. Administration of methylglyoxal bis(guanylhydrazone) [459-86-9] to castrated androgen-treated rats resulted in a marked increase in concns. of all prostatic polyamines. Prostatic ornithine decarboxylase activity was nearly 2-fold and adenosylmethionine decarboxylase activity 9-fold higher than that of the testosterone-treated animals. In contrast with ventral prostate, methylglyoxal bis(guanylhydrazone) treatment moderately inhibited the accumulation of spermidine and spermine [71-44-3] in seminal vesicle, although both ornithine decarboxylase and S-adenosylmethionine decarboxylase activities were stimulated. Difluoromethylornithine inhibited the weight gain of ventral prostate, but methylglyoxal bis(guanylhydrazone) produced a substantial increase in prostatic weight. These changes were largely due to the fact that the volume of prostatic secretion was greatly decreased by difluoromethylornithine, whereas methylglyoxal bis(guanylhydrazone) increased the amount of secretion. Treatment with difluoromethylornithine strikingly increased the methylglyoxal bis(guanylhydrazone) content of both ventral prostate and seminal vesicle, but even under these conditions the drug concentration remained low in comparison with other tissues. A combined use of these 2 polyamine anti-metabolites apparently does not necessarily result in a synergistic growth inhibition of the androgen-induced growth of male accessory sexual glands.

L8 ANSWER 24 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1984:132245 CAPLUS Full-text

DOCUMENT NUMBER: 100:132245

TITLE: Differential effect of α -difluoromethylornithine on the in vivo uptake of carbon-14-labeled polyamines and methylglyoxal bis(guanylhydrazone) by a rat prostate-derived tumor

AUTHOR(S): Heston, Warren D. W.; Kadmon, Dov; Covey, Douglas F.; Fair, William R.

CORPORATE SOURCE: Sch. Med., Washington Univ., St. Louis, MO, 63110, USA

SOURCE: Cancer Research (1984), 44(3), 1034-40

CODEN: CNREA8; ISSN: 0008-5472

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The uptake of exogenously administered radiolabeled polyamines by a rat prostate-derived tumor line, the Dunning R3327 MAT-Lu, and various normal tissues was studied. Pretreatment of tumor cells in vitro with α -difluoromethylornithine (DFMO) [70052-12-9], a polyamine synthesis inhibitor, increased the uptake of both ¹⁴C-labeled putrescine [110-60-1] and spermidine [124-20-9]. The in vitro uptake of [¹⁴C]putrescine by these cells was inhibited by unlabeled putrescine, spermine [71-44-3], spermidine, 1,8-diaminooctane [373-44-4], 1,7-diaminoheptane [646-19-5], 1,6-diaminohexane [124-09-4], 1,5-diaminopentane [462-94-2], and 1,4-diaminopentane [591-77-5], but less effectively by 1,4-diamino-2,3-butene [18231-61-3], and 1,4-diamino-2,3-butyne [53878-96-9]. The diamines, 1,3-diaminopropane [109-76-2] and 1,2-diaminoethane [107-15-3], did not inhibit [¹⁴C]putrescine uptake. When tumor-bearing animals were pretreated with DFMO or with DFMO and 5- α -dihydrotestosterone propionate [855-22-1], the tumor and prostate uptake of [¹⁴C]putrescine and [¹⁴C]cadaverine was enhanced but not substantially increased in other tissues. In contrast to the in vitro results, spermidine and spermine uptakes were not enhanced substantially by DFMO pretreatment into any tissue, and their uptake into the tumor actually decreased. Ethylenediamine, which does not utilize the polyamine transport system, did not have its uptake increased into any tissue following DFMO pretreatment. The chemotherapeutic agent, methylglyoxal bis(guanylhydrazone) [459-86-9], which utilizes the polyamine transport system for uptake into cells, exhibited uptake behavior different from that of the polyamines. Thus, methylglyoxal bis(guanylhydrazone) uptake into the tumor was not significantly increased or decreased by DFMO or by DFMO + 5- α -dihydrotestosterone propionate pretreatment, and only the ventral, but not the dorsal-lateral, lobe of the prostate showed increased uptake of methylglyoxal bis(guanylhydrazone) following DFMO + 5- α -dihydrotestosterone propionate pretreatment.

L8 ANSWER 25 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1983:605764 CAPLUS Full-text

DOCUMENT NUMBER: 99:205764

TITLE: Antigrowth effect of polyamine biosynthesis inhibitors on rat prostate cancer

AUTHOR(S): Herr, Harry W.; Dunzendorfer, Udo; Kleinert, Edward; Whitmore, Willet F., Jr.

CORPORATE SOURCE: Urol. Res. Lab., Sloan-Kettering Inst. Cancer Res., New York, NY, USA

SOURCE: Surgical Forum (1982), 33, 632-4

CODEN: SUFOAX; ISSN: 0071-8041

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Rats bearing s.c. prostatic adenocarcinoma were given either α -difluoromethylornithine (DFMO) [70052-12-9] (1 g/kg), methylglyoxal bisguanylhydrazone (MGBG) [459-86-9] (40 mg/kg, i.p.), or a combination of DFMO + MGBG, daily for 21 days. MGBG alone exhibited tumor growth but was highly toxic. DFMO had little effect, but it reduced the toxicity and potentiated the activity of MGBG (57% cure rate). Only DFMO + MGBG reduced tumor levels of putrescine [110-60-1], spermidine [124-20-9], and spermine [71-44-3].

L8 ANSWER 26 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1983:213331 CAPLUS Full-text

DOCUMENT NUMBER: 98:213331

TITLE: Aspects of polyamine metabolism in relationship to S-adenosylmethionine metabolism revealed by the use of α -difluoromethylornithine, an effective inhibitor of putrescine biosynthesis

AUTHOR(S): Mamont, Pierre S.; Danzin, Charles; Wagner, Joseph

CORPORATE SOURCE: Cent. Rech., Merrell Int., Strasbourg, 67084, Fr.

SOURCE: Biochem. S-Adenosylmethionine Relat. Compd., Proc. Conf. (1982), Meeting Date 1981, 557-65. Macmillan: London, UK.

CODEN: 49REAA

DOCUMENT TYPE: Conference

LANGUAGE: English

AB In rats and rat hepatoma cultures treated with DL- α -difluoromethylornithine, an inhibitor of L-ornithine decarboxylase, reduced polyamine levels were accompanied by increased S-adenosylmethionine (SAM) methyltransferase (I) activity and decarboxylated SAM (dc-SAM) accumulation. The maximum effect was observed in the ventral prostate (.apprx.400-fold increase in dc-SAM content). SAM content was not altered. Accumulation of dc-SAM resulted from substrate limitation for spermidine and spermine synthase reaction, as well as from increased I activity, as normal levels of dc-SAM were restored following polyamine treatment. When depleted cells were exposed to putrescine, the SAM content decreased. The reduced cell growth rate induced by the inhibitor apparently resulted from decreased polyamine synthesis and not dc-SAM accumulation.

L8 ANSWER 27 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1982:197062 CAPLUS Full-text

DOCUMENT NUMBER: 96:197062

TITLE: Accumulation of decarboxylated S-adenosyl-L-methionine in mammalian cells as a consequence of the inhibition of putrescine biosynthesis

AUTHOR(S): Mamont, Pierre S.; Danzin, Charles; Wagner, Joseph; Siat, Marlyse; Joder-Ohlenbusch, Anne Marie; Claverie, Nicole

CORPORATE SOURCE: Cent. Rech., Merrell Int., Strasbourg, Fr.

SOURCE: European Journal of Biochemistry (1982), 123(3), 499-504

CODEN: EJBCAI; ISSN: 0014-2956

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Under normal conditions, decarboxylated S-adenosyl-L-methionine, the aminopropyl donor for polyamine biosynthesis, does not accumulate because of its rapid utilization in spermidine and spermine synthesis. Alteration of polyamine synthesis by DL- α -difluoromethylornithine, an enzyme-activated irreversible inhibitor of L-ornithine decarboxylase, leads to a striking

accumulation of decarboxylated S-adenosyl-L-methionine-L-methionine in rat hepatoma cells cultured in vitro and in rat ventral prostate. This increase is due both to lack of putrescine and spermidine for the aminopropyltransferase reactions and to the elevation of S-adenosyl-L-methionine decarboxylase activity. The biol. implications of accumulation of decarboxylated S-adenosyl-L-methionine are discussed with regard to the regulation of S-adenosyl-L-methionine decarboxylase activity and to the antiproliferative effects of DL- α -difluoromethylornithine.

L8 ANSWER 28 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1982:178544 CAPLUS Full-text

DOCUMENT NUMBER: 96:178544

TITLE: Effect on prostatic growth of 2'-difluoromethylornithine, an effective inhibitor of ornithine decarboxylase

AUTHOR(S): Danzin, Charles; Claverie, Nicole; Wagner, Joseph; Grove, Jeffrey; Koch-Weser, Jan

CORPORATE SOURCE: Cent. Rech., Merrell Int., Strasbourg, 67084, Fr.

SOURCE: Biochemical Journal (1982), 202(1), 175-81

CODEN: BIJOAK; ISSN: 0306-3275

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Difluoromethylornithine (I) given to adult rats in drinking water (20 g/L) for 3 consecutive days caused an 80% decrease in putrescine and spermidine concns. in the ventral prostate and a 36% decrease in spermine concentration. Concomitantly, there was a 7-fold increase in S-adenosylmethionine decarboxylase activity and a 450-fold increase in decarboxylated S-adenosylmethionine concentration. When I was given to immature rats for 12 consecutive days, the above changes were accompanied by a marked reduction in the age-dependent increase in the wet weight and RNA and DNA contents of the ventral prostate. In adult rats I reduced the weight and RNA content of the ventral prostate within 4 days by 32 and 24%, resp., and kept them constant for the next 19 days. Cytol. studies showed that I reduced the size of both prostatic acini and the epithelial cells lining the acini.

L8 ANSWER 29 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1979:568754 CAPLUS Full-text

DOCUMENT NUMBER: 91:168754

TITLE: Effects of α -difluoromethylornithine, an enzyme-activated irreversible inhibitor of ornithine decarboxylase, on testosterone-induced regeneration of prostate and seminal vesicle in castrated rats

AUTHOR(S): Danzin, Charles; Jung, Michel J.; Claverie, Nicole; Grove, Jeffrey; Sjoerdsma, Albert; Koch-Weser, Jan

CORPORATE SOURCE: Cent. Rech. Merrell Int., Strasbourg, 67084, Fr.

SOURCE: Biochemical Journal (1979), 180(3), 507-13

CODEN: BIJOAK; ISSN: 0306-3275

DOCUMENT TYPE: Journal

LANGUAGE: English

AB In adult castrated rats with decreased amts. of polyamines and nucleic acids in the ventral prostate and seminal vesicle, repeated doses of α -difluoromethylornithine (I) [67037-37-0] (200 mg/kg, i.p.) totally blocked the testosterone propionate. (II) [57-85-2] (1 mg, s.c.)-induced increase of putrescine [110-60-1] and spermidine [124-20-9] in the ventral prostate and of putrescine in the seminal vesicle. I slowed the accumulation of spermine [71-44-3] in the ventral prostate and of spermidine in the seminal vesicle. I

also retarded the II-induced accumulation of RNA in the ventral prostate. However, no clear correlation was apparent between accumulation of polyamines and of nucleic acids in the 2 organs. I slowed the II-induced weight gain of the prostate, but not of the seminal vesicle. Cytol. studies suggest that the effect of I on the prostate may be due to inhibition of the II-induced restoration of the secretion content of prostatic acini.

L8 ANSWER 30 OF 42 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1978:440088 CAPLUS Full-text

DOCUMENT NUMBER: 89:40088

TITLE: Anti-proliferative properties of DL- α -difluoromethyl ornithine in cultured cells. A consequence of the irreversible inhibition of ornithine decarboxylase

AUTHOR(S): Mamont, Pierre S.; Duchesne, Marie Christine; Grove, Jeffrey; Bey, Philippe

CORPORATE SOURCE: Cent. Rech., Merrell Int., Strasbourg, Fr.

SOURCE: Biochemical and Biophysical Research Communications (1978), 81(1); 58-66

CODEN: BBRC9; ISSN: 0006-291X

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Both DL- α -methylornithine (I), a competitive inhibitor of ornithine decarboxylase (EC 4.1.1.17) and DL- α -difluoromethylornithine (II), a catalytic irreversible inhibitor of this enzyme, decreased the concns. of putrescine and spermidine but not of spermine in rat hepatoma cells and in mouse leukemia cells cultured in vitro. The depletion of the 2 amines was followed by a striking decrease in the rate of cell replication in both cell lines. Growth of human prostate adenoma cells was also inhibited by II but not I, illustrating the greater effectiveness of the irreversible inhibitor. Putrescine and spermidine may have an essential role in cell division processes.

L8 ANSWER 31 OF 42 USPATFULL on STN

ACCESSION NUMBER: 2000:27745 USPATFULL Full-text

TITLE: Method for isolation of extrachromosomal amplified genes

INVENTOR(S): Wahl, Geoffrey M., San Diego, CA, United States
Shimizu, Noriaki, San Diego, CA, United States

PATENT ASSIGNEE(S): The Salk Institute for Biological Studies, La Jolla, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE
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PATENT INFORMATION:	US 6033849		20000307
APPLICATION INFO.:	US 1996-704391		19960826 (8)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1995-452275, filed on 26 May 1995, now abandoned		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Horlick, Kenneth R.		
LEGAL REPRESENTATIVE:	Gray Cary Ware & Freidenrich LLP, Haile, Lisa A.		
NUMBER OF CLAIMS:	12		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	7 Drawing Figure(s); 6 Drawing Page(s)		
LINE COUNT:	846		
CAS INDEXING IS AVAILABLE FOR THIS PATENT.			

AB The present invention provides a method for the isolation of extrachromosomal amplified nucleic acids that are associated with a cell proliferative disorder. Isolation and further identification of such genes is critical for diagnosis, prognosis, and course of therapy.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L8 ANSWER 32 OF 42 USPATFULL on STN

ACCESSION NUMBER: 1999:40478 USPATFULL Full-text
TITLE: Conformationally restricted polyamines
INVENTOR(S): Frydman, Benjamin J., Madison, WI, United States
Marton, Laurence J., Fitchburg, WI, United States
Reddy, Vendohar K., Madison, WI, United States
Valasinas, Aldonia L., Madison, WI, United States
Witiak, Donald T., Madison, WI, United States
PATENT ASSIGNEE(S): Wisconsin Alumni Research Foundation, Madison, WI,
United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5889061		19990330
APPLICATION INFO.:	US 1997-951015		19971015 (8)

	NUMBER	DATE
PRIORITY INFORMATION:	US 1996-28680P	19961018 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	Granted	
PRIMARY EXAMINER:	Burn, Brian M.	
LEGAL REPRESENTATIVE:	DeWitt Ross & Stevens S.C.	
NUMBER OF CLAIMS:	24	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	32 Drawing Figure(s); 20 Drawing Page(s)	
LINE COUNT:	1639	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Compounds of Formula I:

E-NH-D-NH-B-A-B-NH-D-NH-E

(I)

wherein A is C.sub.2 -C.sub.6 alkene, C.sub.3 -C.sub.6 cycloalkyl, cycloalkenyl, or cycloaryl; B is independently a single bond, C.sub.1 -C.sub.6 alkyl alkenyl; D is independently C.sub.1 -C.sub.6 alkyl or alkenyl, or C.sub.3 -C.sub.6 cycloalkyl, cycloalkenyl, or cycloaryl; and E is independently H, C.sub.1 -C.sub.6 alkyl or alkenyl; and pharmaceutically-suitable salts thereof; a synthetic method therefor, pharmaceutical dosage forms containing one of more of these compounds, and use of these compounds in the treatment of neoplastic cell growth, are disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L8 ANSWER 33 OF 42 USPATFULL on STN

ACCESSION NUMBER: 97:94282 USPATFULL Full-text
TITLE: Inhibition of cancer cell growth, proliferation, and metastasis using N,N'- α,ω -diaminoalkanes
INVENTOR(S): Frydman, Benjamin J., Madison, WI, United States
PATENT ASSIGNEE(S): Wisconsin Alumni Research Foundation, Madison, WI,

United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5677350		19971014
APPLICATION INFO.:	US 1995-472431		19950607 (8)
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Goldberg, Jerome D.		
LEGAL REPRESENTATIVE:	DeWitt Ross & Stevens SC		
NUMBER OF CLAIMS:	18		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	32 Drawing Figure(s); 25 Drawing Page(s)		
LINE COUNT:	871		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to the inhibition of cancer cell growth, proliferation, and metastasis by contacting cells with an N,N'-dibenzyl α,ω -diaminoalkane, a derivative of naturally-occurring putrescine. More specifically, the present invention relates to the treatment of cancer in humans by administration of a cancer cell growth-inhibiting amount of an N,N'-dibenzyl α,ω -diaminoalkane to a human cancer patient.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L8 ANSWER 34 OF 42 USPATFULL on STN

ACCESSION NUMBER: 97:25070 USPATFULL Full-text
 TITLE: Method of controlling tumor growth rate
 INVENTOR(S): Bey, Philippe, Strasbourg, France
 Jung, Michel, Graffenstaden, France
 PATENT ASSIGNEE(S): Marion Merrell et Compagnie C/O Merrell Pharmaceuticals Inc., Cincinnati, OH, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5614557		19970325
APPLICATION INFO.:	US 1995-403531		19950314 (8)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1994-284706, filed on 2 Aug 1994, now abandoned which is a continuation of Ser. No. US 1993-137397, filed on 14 Oct 1993, now abandoned which is a continuation of Ser. No. US 1993-2521, filed on 11 Jan 1993, now abandoned which is a continuation of Ser. No. US 1992-874989, filed on 24 Apr 1992, now abandoned which is a continuation of Ser. No. US 1991-759633, filed on 12 Sep 1991, now abandoned which is a continuation of Ser. No. US 1990-534008, filed on 1 Jun 1990, now abandoned which is a continuation of Ser. No. US 1989-431685, filed on 3 Nov 1989, now abandoned which is a continuation of Ser. No. US 1989-334733, filed on 6 Apr 1989, now abandoned which is a continuation of Ser. No. US 1988-228789, filed on 4 Aug 1988, now abandoned which is a continuation of Ser. No. US 1987-110639, filed on 15 Oct 1987, now abandoned which is a continuation of Ser. No. US 1984-639977, filed on 10 Aug 1984, now abandoned which is a division of Ser. No. US 1982-382265, filed on 26 May 1982, now abandoned which is a continuation of Ser. No. US 1981-262834, filed on 12 May 1981, now abandoned which is a continuation-in-part of Ser. No. US 1980-204749, filed on 7 Nov 1980, now abandoned which		

is a continuation of Ser. No. US 1979-28757, filed on 10 Apr 1979, now abandoned which is a continuation-in-part of Ser. No. US 1977-814765, filed on 11 Jul 1977, now abandoned

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Goldberg, Jerome D.
LEGAL REPRESENTATIVE: Wille, Louis J.
NUMBER OF CLAIMS: 3
EXEMPLARY CLAIM: 1
LINE COUNT: 998

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB α -Fluoromethyl- or α -difluoromethylornithine, and certain derivatives thereof, can be used alone or in combination with cytotoxic agents for the treatment of neoplastic diseases.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L8 ANSWER 35 OF 42 USPATFULL on STN

ACCESSION NUMBER: 95:90332 USPATFULL Full-text
TITLE: Polyamine-polyamine and polyamine-protein transport inhibitor conjugates and their use as pharmaceuticals and in research relating to polyamine transport
INVENTOR(S): Aziz, Shewan M., Lexington, KY, United States
Gillespie, Mark N., Lexington, KY, United States
PATENT ASSIGNEE(S): The University of Kentucky Research Foundation, Lexington, KY, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5456908		19951010
APPLICATION INFO.:	US 1994-203629		19940301 (8)
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Kishore, Gollamudi S.		
LEGAL REPRESENTATIVE:	Burns, Doane, Swecker & Mathis		
NUMBER OF CLAIMS:	15		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	13 Drawing Figure(s); 5 Drawing Page(s)		
LINE COUNT:	1546		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Novel classes of inhibitors which selectively inhibit the cellular transport of normally transported substances, specifically polyamines are taught which comprise (i) polymers of the transported substance or (ii) protein or polypeptide conjugates of the transported substance. These inhibitors may be used in vitro to assess the effect of the transported substance on cellular functions and in vivo for treating disease conditions involving transport of the particular substance, e.g., a polyamine.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L8 ANSWER 36 OF 42 USPATFULL on STN

ACCESSION NUMBER: 91:24589 USPATFULL Full-text
TITLE: Treatment of tumors with autologous LAK cells, interleukin-2 and an ornithine decarboxylase inhibitor
INVENTOR(S): Bowlin, Terry L., Maineville, OH, United States
Sunkara, Sai P., Cincinnati, OH, United States
PATENT ASSIGNEE(S): Merrell Dow Pharmaceuticals, Cincinnati, OH, United

States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5002879		19910326
APPLICATION INFO.:	US 1989-449288		19891205 (7)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1988-271371, filed on 14 Nov 1988, now abandoned which is a continuation of Ser. No. US 1986-860166, filed on 6 May 1986, now abandoned		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Stone, Jacqueline		
LEGAL REPRESENTATIVE:	Nesbitt, Stephen L.		
NUMBER OF CLAIMS:	2		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	1 Drawing Figure(s); 1 Drawing Page(s)		
LINE COUNT:	394		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Ornithine decarboxylase inhibitors when administered in conjunction with autologous LAK cells and interleukin-2 provide for an enhanced treatment of neoplastic disease states. This enhancement is provided by the ability of an ornithine decarboxylase inhibitor to reduce tumor load and to enhance interleukin-2 production in T helper cells.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L8 ANSWER 37 OF 42 USPATFULL on STN

ACCESSION NUMBER: 90:38408 USPATFULL Full-text
TITLE: AziridinyI putrescine containing compositions and their uses in treating prostate cancer
INVENTOR(S): Heston, Warren D. W., Montrose, NY, United States
PATENT ASSIGNEE(S): Sloan-Kettering Institute for Cancer Research, New York, NY, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 4925835		19900515
APPLICATION INFO.:	US 1987-113550		19871026 (7)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1986-858348, filed on 1 May 1986, now abandoned which is a continuation of Ser. No. US 1984-700644, filed on 12 Feb 1984, now abandoned		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Howard, Jacqueline V.		
ASSISTANT EXAMINER:	Medley, Margaret B.		
LEGAL REPRESENTATIVE:	White, John P.		
NUMBER OF CLAIMS:	29		
EXEMPLARY CLAIM:	1,21		
NUMBER OF DRAWINGS:	4 Drawing Figure(s); 4 Drawing Page(s)		
LINE COUNT:	661		

AB This invention relates to methods of inhibiting the proliferation of prostate cancer cells comprising contacting the cells with an effective amount of a cytotoxic polyamine compound.

The invention also relates to methods of inhibiting the proliferation of prostate cancer cells in a subject afflicted with prostate cancer.

The invention further concerns therapeutic compositions comprising an effective prostate cancer cell proliferation inhibiting amount of 1-(4-aminobutyl) aziridine and a pharmaceutically acceptable carrier.

The invention also concerns two-component therapeutic compositions.

L8 ANSWER 38 OF 42 USPATFULL on STN

ACCESSION NUMBER: 89:34520 USPATFULL Full-text
TITLE: S-alkylated coenzyme A with effect on polyamine acetylase
INVENTOR(S): Pegg, Anthony E., Hummelstown, PA, United States
Erwin, Bradley G., Hershey, PA, United States
PATENT ASSIGNEE(S): Research Corporation, New York, NY, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 4826968		19890502
APPLICATION INFO.:	US 1985-727508		19850426 (6)
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Griffin, Ronald W.		
ASSISTANT EXAMINER:	Crane, L. Eric		
LEGAL REPRESENTATIVE:	Scully, Scott, Murphy & Presser		
NUMBER OF CLAIMS:	3		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	2 Drawing Figure(s); 2 Drawing Page(s)		
LINE COUNT:	496		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to the novel compound N-[2-(S-Coenzyme A) acetyl] sym-norspermidine which electively inhibits the enzyme spermidine/spermine N.sup.1 acetyl transferase thereby aberrating the polyamine biosynthesis pathway. The present compound alone or in combination with other agents can be employed in pharmaceutically acceptable compositions and in convenient dosage forms for use in the treatment of neoplastic diseases, diseases caused by parasitic protozoans, diseases involving deranged cell growth or other related diseases.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L8 ANSWER 39 OF 42 USPATFULL on STN

ACCESSION NUMBER: 85:8954 USPATFULL Full-text
TITLE: Process for treating diseases with ODC inhibitors
INVENTOR(S): Sunkara, Sai P., Cincinnati, OH, United States
Prakash, Nellikunja J., Cincinnati, OH, United States
PATENT ASSIGNEE(S): Merrell Dow Pharmaceuticals Inc., Cincinnati, OH, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 4499072		19850212
APPLICATION INFO.:	US 1983-460224		19830124 (6)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1982-445349, filed on 29 Nov 1982, now abandoned		

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Hazel, Blondel
LEGAL REPRESENTATIVE: McDonald, Raymond A., Nesbitt, Stephen L., Street, Gary D.
NUMBER OF CLAIMS: 15
EXEMPLARY CLAIM: 1
LINE COUNT: 538

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention relates to the improvement of the polyamine depletion effects of ornithine decarboxylase inhibitors and/or S-adenosylmethionine decarboxylase inhibitors, the improvement being effected by the use of interferon in conjunctive therapy with said inhibitors.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L8 ANSWER 40 OF 42 USPATFULL on STN

ACCESSION NUMBER: 83:50809 USPATFULL Full-text
TITLE: 2-(Difluoromethyl)-2,5-diaminopentanoic acid
INVENTOR(S): Bey, Philippe, Strasbourg, France
Jung, Michel, Illkirch-Graffenstaden, France
PATENT ASSIGNEE(S): Merrell Toraude et Compagnie, Strasbourg, France
(non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 4413141		19831101
APPLICATION INFO.:	US 1982-419347		19820917 (6)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1979-53937, filed on 2 Jul 1979, now abandoned which is a continuation of Ser. No. US 1977-814765, filed on 11 Jul 1977, now abandoned		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Raymond, Richard		
LEGAL REPRESENTATIVE:	Frankhouser, David E., McDonald, Raymond A., Street, Gary D.		
NUMBER OF CLAIMS:	3		
EXEMPLARY CLAIM:	1		
LINE COUNT:	565		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention relates to 2-(difluoromethyl)-2,5-diaminopentanoic acid, or a pharmaceutically acceptable acid addition salt thereof, and to the methods for the preparation and use thereof.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L8 ANSWER 41 OF 42 USPATFULL on STN

ACCESSION NUMBER: 82:24084 USPATFULL Full-text
TITLE: Method of treating benign prostatic hypertrophy
INVENTOR(S): Bey, Philippe, Strasbourg, France
Jung, Michel, Illkirch Groffenstaden, France
PATENT ASSIGNEE(S): Merrell-Toraude et Cie, Strasbourg, France (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 4330559		19820518

APPLICATION INFO.: US 1981-231072 19810203 (6)
RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1979-28739, filed
on 10 Apr 1979, now abandoned which is a
continuation-in-part of Ser. No. US 1977-814765, filed
on 11 Jul 1977, now abandoned
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Goldberg, Jerome D.
LEGAL REPRESENTATIVE: Frankhouser, David E., McDonald, Raymond A., Stein,
William J.
NUMBER OF CLAIMS: 8
EXEMPLARY CLAIM: 1
LINE COUNT: 853
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB There is described a method for treating benign prostatic hypertrophy
comprising the administration of 2,5-di-amino-2-(mono-,di-, or
trifluoromethyl)pentanoic acid or derivative thereof.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L8 ANSWER 42 OF 42 USPATFULL on STN
ACCESSION NUMBER: 82:912 USPATFULL Full-text
TITLE: Method for controlling fertility in mammals
INVENTOR(S): Bey, Philippe, Strasbourg, France
Jung, Michel, Illkirch Graffenstaden, France
PATENT ASSIGNEE(S): Merrell Toraude et Compagnie, Strasbourg, France
(non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 4309442		19820105
APPLICATION INFO.:	US 1980-212473		19801203 (6)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1979-58476, filed on 18 Jul 1979, now abandoned which is a continuation-in-part of Ser. No. US 1977-814765, filed on 11 Jul 1977, now abandoned		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Schenkman, Leonard		
LEGAL REPRESENTATIVE:	Frankhouser, David E.		
NUMBER OF CLAIMS:	8		
EXEMPLARY CLAIM:	1		
LINE COUNT:	1099		
CAS INDEXING IS AVAILABLE FOR THIS PATENT.			
AB	A method for preventing gestation in mammals comprising the administration of a 2,5-diamino-2-halomethylpentanoic acid or derivative thereof.		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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(FILE 'HOME' ENTERED AT 08:41:35 ON 11 OCT 2006)

FILE 'MEDLINE, WPIDS, CAPLUS, USPATFULL' ENTERED AT 08:41:56 ON 11 OCT
2006

L1 4393 S "DMFO" OR "DIFLUOROMETHYLORNITHINE"
L2 0 S "DECREAS? SPERMINE" OR "DECREAS? SPERMIDINE"

L3	1364 S L1 AND SPERMINE
L4	1669 S L1 AND SPERMIDINE
L5	1137 S L3 NOT PY>2000
L6	36 S L5 AND DECREASING
L7	0 S PROSTATE AND L5
L8	42 S PROSTATE AND L5

---Logging off of STN---